

REMARKS

I. Status of the Claims

Claims 18-34 are pending in this application. Claims 18 and 31 have been amended to more precisely define that which Applicants consider to be their invention and to correct typographical errors, as follows:

In claim 18, the terms "C₃-C₆ cycloalkyl groups" and "a methyl group" have been deleted and the term "a (C₃-C₆)cycloalkylmethyl group" has been inserted in their place. Support for this amendment can be found, for example, on page 270, lines 22-23, of the specification as-filed.

The term "a benzyl group" has been added to claim 18. Support for this amendment can be found, for example, at page 271, line 8, of the specification as-filed.

Applicants have amended the definition of R° found in claim 18. Support for this amendment can be found, for example, on page 269, line 19 through page 270, line 4, of the specification as-filed.

In claim 31, Applicants have added the definition of R₅ to section (A). Support for this amendment can be found, for example, on page 282, line 16 through page 283, line 7, and on page 9, lines 1-4, of the specification as-filed.

In claim 31, Applicants have made it clear that Ra in section (C) is a methyl group or an ethyl group. Support for this amendment can be found, for example, on page 29, lines 10-14, of the specification as-filed.

In both claims 18 and 31, Applicants have corrected inadvertent typographical errors by amending the terms "heterocycyl" and "heterocyclcyamino" to respectively to read "heterocyclyl" and "heterocycllamino."

No new matter has been introduced by these amendments, nor do these amendments raise new issues or necessitate the undertaking of any additional search of the art by the Office. Accordingly, their entry is respectfully requested.

II. Correspondence Address

Further to the request of February 26, 2001, Applicants again respectfully request that for all future correspondence concerning this application the Office use the address and telephone number provided in the Grant of Power of Attorney, filed on February 26, 2001, which is as follows:

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III. Restriction Requirement

Applicants' claims 18-34 are subject to a restriction requirement under 35 U.S.C. § 121. (Office Action dated December 11, 2001, pages 2-3.) The Examiner has grouped the claims as follows:

Group I: Claims 18-25 and 31, drawn to compounds;
Group II: Claims 26-30, drawn to a method of making compounds; and
Group III: Claims 32-34, drawn to a binary mixture of compounds.

Applicants respectfully traverse this requirement. For a restriction requirement to be proper, the Examiner must set forth the reasons why the inventions *as claimed* are either independent or distinct and the reasons for insisting upon restriction. M.P.E.P. § 808 (emphasis in original). The Examiner has done neither in this case.

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For example, the *Manual of Patent Examining Procedure (MPEP)* provides a test for determining whether a process of making is distinct from the product made:

A process of making and a product made by the process can be shown to be distinct inventions if either or both of the following can be shown: (A) that the process *as claimed* is not an obvious process of making the product and the process *as claimed* can be used to make other and different products; or (B) that the product *as claimed* can be made by another and materially different process.

M.P.E.P. § 806.05(f) (8th ed., August 2001) (emphasis in original). The Examiner, in the present case, has not shown, nor even alleged, any facts that would indicate that Groups I-III as outlined above are either independent or distinct from one another. Thus, the Examiner has not met his burden of showing distinctness. For this reason alone the restriction requirement is improper.

In addition to showing distinctness, however, a proper restriction requirement requires the Examiner to show that a *prima facie* case of a serious burden exists. M.P.E.P. § 803. The Examiner "must show by appropriate explanation one of the following: (A) [s]eparate classification . . . separate status in the art . . . [or] a different field of search." M.P.E.P. § 808.02 (emphasis supplied). The Examiner has made no attempt to satisfy this additional and independent burden in this case either.

Accordingly, because the Examiner has failed to present a *prima facie* case that the inventions are distinct and has failed to even allege that a serious burden exists, Applicants respectfully traverse the restriction requirement. However, to be fully responsive, Applicants elect, with traverse, the subject matter of Group I, claims 18-25 and 31, for prosecution on the merits. Further, Applicants thank the Examiner for the acknowledgement that "in the event that Group I is elected, and claims therein found

allowable, the corresponding method-of-making claims will be rejoined for further examination." (Office Action dated December 11, 2001, page 2, lines 11-13.)

Applicants respectfully request that the Examiner pursue this course upon determination of the allowability of the claims of the elected Group.

Applicants do not make any statement regarding the obviousness of one group, as grouped by the Examiner, relative to the other, nor should one be inferred. Applicants merely assert that the search of all the pending claims would not be unduly burdensome. Accordingly, the restriction requirement should be withdrawn.

IV. Election Requirement

Under 35 U.S.C. § 121, the Examiner has additionally required Applicants to elect, from Group I above, a disclosed species for prosecution on the merits and to provide the Examiner with the chemical structure of the elected species. (Office Action dated December 11, 2001, page 3.) Applicants respectfully traverse this election of species requirement. To be fully responsive, however, Applicants, with traverse, elect 2"-methylpyrido[2,3-5 γ ,5 δ]pristinamycin I_E (as shown, for example, in the specification, at page 36, line 19; and in claims 18, 19, 21, 26, 27, 29, 30, 32, 33, and 34) for the species of Group I.

Applicants traverse this requirement on the ground that it would not be unduly burdensome for the Examiner to conduct a search for all the claimed compounds of Group I, as it is likely that art encompassing the elected species would also encompass the other claimed species. Applicants do not make any statement regarding the obviousness of one species relative to any other, nor should one be inferred.

Applicants merely assert that a search of all the claimed species would not be unduly burdensome.

Accordingly, Applicants respectfully request that all of the claimed species be examined in this application. If the Examiner chooses to maintain the election requirement, Applicants expect the Examiner, if the elected species is found allowable, to continue to examine the full scope of the elected subject matter to the extent necessary to determine the patentability thereof, and then to extend the search to a reasonable number of the non-elected species, as is the Examiner's duty according to M.P.E.P. § 803.02 and 35 U.S.C. § 121. In any case, the election of species requirement should be withdrawn in view of the foregoing remarks.

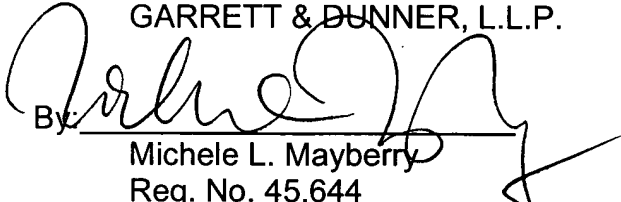
V. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: March 11, 2002

Attachment: Appendix (Version With Markings to Show Changes Made)

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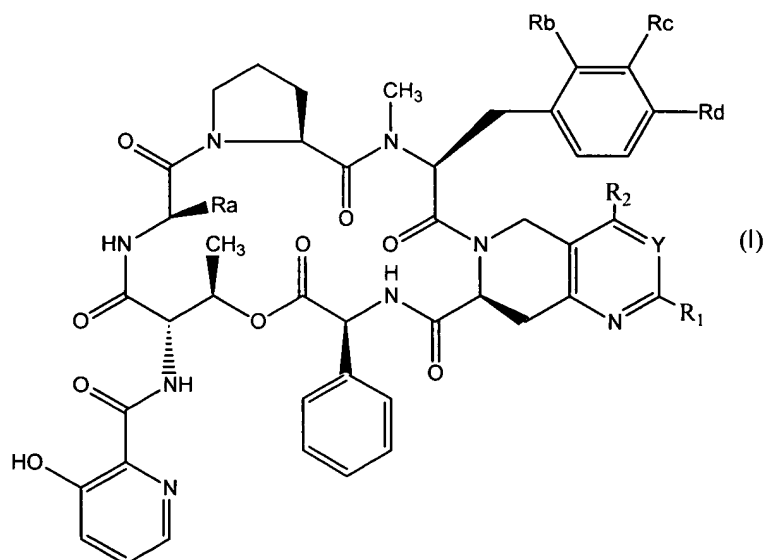
APPENDIX TO AMENDMENT OF MARCH 11, 2002

Version with Markings to Show Changes Made

IN THE CLAIMS:

Please replace pending claims 18 and 31 with the respective amended versions thereof, as follows:

18. (Once Amended) A group B streptogramin derivative of formula (I) or a salt thereof:



wherein:

(A) Y is chosen from (i) a nitrogen atom and (ii) =CR₃- groups, and

(1) when Y is chosen from =CR₃- groups, R₁ is chosen from

(a₁) a hydrogen atom, C₁-C₈ alkyl groups, and C₂-C₈ alkenyl groups,

- (b₁) C₃-C₈ cycloalkyl groups, and saturated and unsaturated C₃-C₈ heterocyclyl groups,
- (c₁) an unsubstituted phenyl group,
- (d₁) a phenyl group substituted with at least one substituent chosen from halogen atoms, a hydroxyl group, alkyl groups, alkyloxy groups, alkylthio groups, alkylsulphinyl groups, alkylsulphonyl groups, an amino group, alkylamino groups, and dialkylamino groups, and
- (e₁) groups -NR'R'', wherein
 - R' and R'', which are identical or different, are each chosen from a hydrogen atom, and C₁-C₃ alkyl groups, or
 - R' and R'', which are identical or different, form, together with the nitrogen atom to which they are attached, a 3- to 8-membered heterocyclyl group, wherein one of said members, in addition to said nitrogen atom, may be an atom chosen from an oxygen atom, a sulphur atom, and a nitrogen atom, and wherein said heterocyclyl group is optionally substituted with a group chosen from alkyl groups, C₂-C₈ alkenyl groups, C₃-C₆ cycloalkyl groups, saturated and unsaturated 4- to 6-membered heterocyclyl groups, a benzyl group, an unsubstituted phenyl group, and a substituted phenyl group, as defined above in (d₁),
- (f₁) halomethyl groups, a hydroxymethyl group, and alkyloxymethyl groups,

- (g₁) alkylthiomethyl groups, wherein said alkyl portion is optionally substituted with an -NR'R" group, and wherein said R' and said R" are as defined above in (e₁),
- (h₁) alkylsulphinylmethyl groups, alkylsulphonylmethyl groups, an acyloxymethyl group, a benzyloxymethyl group, a cyclopropylaminomethyl group, and -(CH₂)_nNR'R" groups, wherein n is chosen from integers ranging from 1 to 4, and wherein said R' and said R" are as defined above in (e₁), and
- (i₁) when R₃ is a hydrogen atom, R₁ is additionally chosen from a formyl group, a carboxyl group, alkyloxycarbonyl groups, and -CONR'R" groups, wherein said R' and said R" are defined as above in (e₁), and
- (2) when Y is a nitrogen atom, R₁ is chosen from
- (a₂) options (a₁), (b₁), (c₁), (d₁), and (e₁) as defined above, and
- ~~(b₂) -XR° groups, wherein X is chosen from an oxygen atom, a sulphur atom, a sulphinyl group, a sulphonyl group, and an -NH- group, and wherein R° is chosen from~~
- ~~(i) -C₁-C₈ alkyl groups, C₃-C₆ cycloalkyl groups,~~
- ~~(ii) -saturated and unsaturated 3- to 8-membered heterocyclyl groups,~~
- ~~(iii) -3- to 8-membered heterocyclylmethyl groups, wherein said heterocyclyl portion is attached to said methyl group by way of a~~

~~unit chosen from a carbon atom, an unsubstituted phenyl group, and a substituted phenyl group, as defined above in (d₄),~~

~~(iv) — (CH₂)_nNR'R'' groups, wherein said R' and said R'' are defined as above in (e₁) and n is chosen from integers ranging from 2 to 4, and~~

~~(v) — when said X is an —NH— group, R° is additionally chosen from a hydrogen atom,~~

(b₂) —XR° groups, wherein X is chosen from an oxygen atom, a sulphur atom, a sulphinyl group, a sulphonyl group, and an —NH— group, and wherein R° is chosen from (i) (C₁ to C₈) alkyl groups, (ii) (C₃ to C₆) cycloalkyl groups, (iii) saturated and unsaturated 3- to 8-membered heterocyclyl groups, (iv) 3- to 8-membered heterocyclylmethyl groups in which the heterocyclyl portion is attached to the methyl group by a carbon atom, (v) an unsubstituted phenyl group, (vi) phenyl groups substituted with at least one group chosen from halogen atoms, a hydroxyl group, alkyl groups, alkyloxy groups, alkylthio groups, alkylsulfinyl groups, alkylsulfonyl groups, an amino group, alkylamino groups, and dialkylamino groups, (vii) —(CH₂)_nNR'R'' groups, wherein R' and R'' are as defined above in (e₁), and wherein n is chosen from integers ranging from 2 to 4, and (viii) if X is an NH group, R° may also be a hydrogen atom;

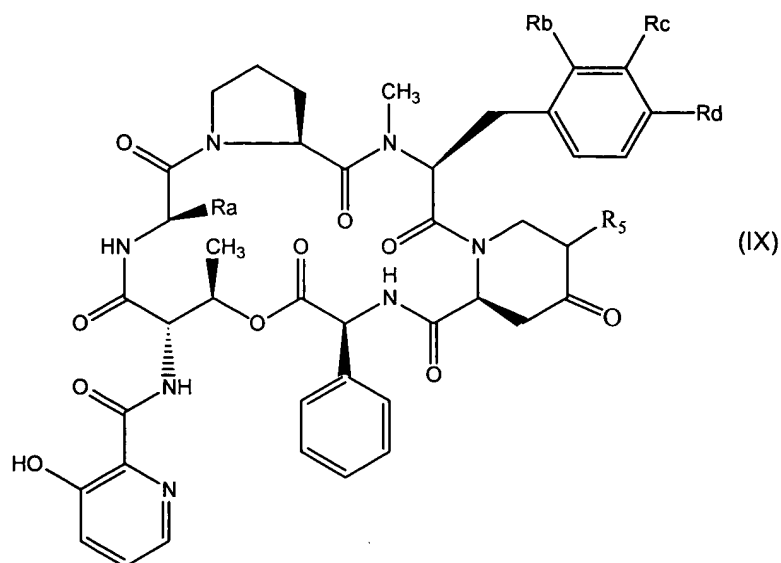
- (B) R_2 is chosen from a hydrogen atom and C_1 - C_3 alkyl groups,
- (C) R_3 is chosen from a hydrogen atom, alkyl groups, a carboxyl group, alkyloxycarbonyl groups, and carbamoyl groups of formula $-\text{CO}-\text{NR}'\text{R}''$, wherein said R' and said R'' are defined as above in (e₁),
- (D) R_a is chosen from a methyl group and an ethyl group, and
- (E) R_b , R_c , and R_d are defined as follows:
- (1) - R_b and R_c are each a hydrogen atom and
- R_d is chosen from a hydrogen atom, a methylamino group, and a dimethylamino group, or
 - (2) - R_b is a hydrogen atom,
- R_c is chosen from a hydrogen atom, a chlorine atom, a bromine atom, and C_3 - C_5 alkenyl groups, and
- R_d is chosen from $-\text{N}(\text{CH}_3)\text{R}'''$ groups, wherein
- R''' is chosen from
 - (a) alkyl groups, C_2 - C_4 hydroxyalkyl groups, and C_2 - C_8 alkenyl groups, wherein said C_2 - C_8 alkenyl groups are optionally substituted with a group chosen from
 - (i) an unsubstituted phenyl group, ~~C_3 - C_6 cycloalkyl groups, a methyl group, a $(C_3$ - C_6)cycloalkylmethyl group~~, a benzyl group, and
 - (ii) a benzyl group substituted with at least one substituent as defined with respect to said substituted phenyl groups in (d₁) above,

- (iii) heterocyclylmethyl groups and heterocyclylethyl groups, wherein said heterocyclyl portions of said heterocyclylmethyl groups and said heterocyclylethyl groups are chosen from saturated and unsaturated 5- to 6-membered heterocyclyl groups comprising from 1 to 2 heteroatoms chosen from a sulphur atom, an oxygen atom, and a nitrogen atom, and wherein said heterocyclyl groups are optionally substituted with a group chosen from alkyl groups, C₂-C₈ alkenyl groups, C₃-C₆ cycloalkyl groups, saturated and unsaturated 4- to 6-membered heterocyclyl groups, an unsubstituted phenyl group, a benzyl group, and a substituted phenyl group as defined above in (d₁),
- (b) a cyanomethyl group, and
- (c) -CH₂COR_e groups, wherein R_e is chosen from
 - (i) -OR'_e groups, wherein R'_e is chosen from a hydrogen atom, C₁-C₆ alkyl groups, C₂-C₆ alkenyl groups, a benzyl group, and heterocyclylmethyl groups, wherein said heterocyclyl portion is chosen from 5- to 6- membered ~~heterocycyl~~ heterocyclyl groups comprising from 1 to 2 heteroatoms chosen from a sulphur atom, an oxygen atom, and a nitrogen atom,

- (ii) alkylamino groups, alkylmethylamino groups, **heterocycleamino** heterocyclylamino groups and heterocyclylmethylamino groups, wherein said heterocyclyl portion of said **heterocycleamino** heterocyclylamino groups and said heterocyclylmethylamino groups is chosen from 5- to 6- membered saturated heterocyclyl groups comprising from 1 to 2 heteroatoms chosen from a sulphur atom, an oxygen atom, and a nitrogen atom, and wherein said heterocyclyl groups are optionally substituted with a group chosen from alkyl groups, a benzyl group, and alkyloxycarbonyl groups, or
- (3) - Rb is a hydrogen atom, and
- Rd is chosen from an -NHCH_3 group and an $\text{-N(CH}_3)_2$ group, and Rc is chosen from a chlorine atom, and a bromine atom, and when Rd is an $\text{-N(CH}_3)_2$ group, Rc is chosen from $\text{C}_3\text{-C}_5$ alkenyl groups, or
- (4) - Rb and Rd are each a hydrogen atom and
- Rc is chosen from halogen atoms, alkylamino groups, dialkylamino groups, alkyloxy groups, a trifluoromethoxy group, thioalkyl groups, $\text{C}_1\text{-C}_6$ alkyl groups, and trihalomethyl groups, or
- (5) - Rb and Rc are each a hydrogen atom and

- Rd is chosen from halogen atoms, an ethylamino group, a diethylamino group, a methylethylamino group, alkyloxy groups, a trifluoromethoxy group, alkylthio groups, alkylsulphinyl groups, alkylsulphonyl groups, C₁-C₆ alkyl groups, a phenyl group, and trihalomethyl groups, or
- (6) - Rb is a hydrogen atom and
 - Rc is chosen from halogen atoms, alkylamino groups, dialkylamino groups, alkyloxy groups, a trifluoromethoxy group, thioalkyl groups, and C₁-C₃ alkyl groups, and
 - Rd is chosen from halogen atoms, an amino group, alkylamino groups, dialkylamino groups, alkyloxy groups, a trifluoromethoxy group, thioalkyl groups, C₁-C₆ alkyl groups, and trihalomethyl groups, or
- (7) - Rc is a hydrogen atom and
 - Rb and Rd are each a methyl group, and
- unless otherwise stated, said alkyl groups, said alkenyl groups, and said acyl groups are chosen from, respectively, straight and branched alkyl groups, straight and branched alkenyl groups, and straight and branched acyl groups, and
- unless otherwise stated, said alkyl groups and said acyl groups comprise from 1 to 4 carbon atoms.

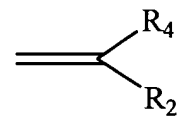
31. (Once Amended) A streptogramin derivative of formula (IX):



wherein

(A) - R_a is a methyl group, and

- R_5 is chosen from disubstituted methylenyl groups of formula:



wherein:

(a) R_2 is chosen from a hydrogen atom and C_1 - C_3 alkyl groups and

R_4 is a hydrogen atom, or

(b) R_2 is a hydrogen atom and

R_4 is chosen from a hydrogen atom and dialkylamino groups,

- R_b , R_c , and R_d are defined as follows:

- (1) - Rb and Rc are each a hydrogen atom, and
- Rd is chosen from a hydrogen atom, a methylamino group, and a dimethylamino group, or
- (2) - Rb is a hydrogen atom,
- Rc is chosen from a hydrogen atom, a chlorine atom, a bromine atom, and C₃-C₅ alkenyl groups, and
 - Rd is chosen from -N(CH₃)R''' groups, wherein
 - R''' is chosen from
 - (a) alkyl groups, C₂-C₄ hydroxyalkyl groups, and C₂-C₈ alkenyl groups, wherein said C₂-C₈ alkenyl groups are optionally substituted with a group chosen from
 - (i) an unsubstituted phenyl group, C₃-C₆ cycloalkyl groups, a methyl group, a benzyl group, **and**
 - (ii) a benzyl group substituted with at least one substituent ~~as defined with respect to said substituted phenyl groups in (d₁) above,~~ chosen from halogen atoms, a hydroxyl group, alkyl groups, alkyloxy groups, alkylthio groups, alkylsulphinyl groups, alkylsulphonyl groups, an amino group, alkylamino groups, and dialkylamino groups,
 - (iii) heterocyclymethyl groups and heterocycylethyl groups, wherein said heterocyclyl portions of said heterocyclymethyl groups and said heterocycylethyl groups are chosen from saturated and

unsaturated 5- to 6-membered heterocyclyl groups comprising from 1 to 2 heteroatoms chosen from a sulphur atom, an oxygen atom, and a nitrogen atom, and wherein said heterocyclyl groups are optionally substituted with a group chosen from alkyl groups, C₂-C₈ alkenyl groups, C₃-C₆ cycloalkyl groups, saturated and unsaturated 4- to 6-membered heterocyclyl groups, an unsubstituted phenyl group, a substituted phenyl group as defined above in ~~(d₄)~~ (a)(ii),

(b) a cyanomethyl group, and

(c) -CH₂COR_e groups, wherein R_e is chosen from

(i) -OR'_e groups, wherein R'_e is chosen from a hydrogen atom, C₁-C₆

alkyl groups, C₂-C₆ alkenyl groups, a benzyl group, and

heterocyclylmethyl groups, wherein said heterocyclyl portion is

chosen from 5- to 6- membered ~~heterocyclyl~~ heterocyclyl

groups comprising from 1 to 2 heteroatoms chosen from a

sulphur atom, an oxygen atom, and a nitrogen atom,

(ii) alkylamino groups, alkylmethylamino groups, ~~heterocyclecyamine~~

heterocyclylamino groups and heterocyclylmethylamino

groups, wherein said heterocyclyl portion of said

~~heterocyclecyamine~~ heterocyclylamino groups and said

heterocyclylmethylamino groups is chosen from 5- to 6-

membered saturated heterocyclyl groups comprising from 1 to 2

heteroatoms chosen from a sulphur atom, an oxygen atom, and

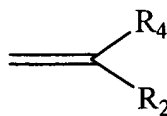
a nitrogen atom, and wherein said heterocyclyl groups are optionally substituted with a group chosen from alkyl groups, a benzyl group, and alkyloxycarbonyl groups, or

- (3) - Rb is a hydrogen atom, **and**
- Rd is chosen from an -NHCH_3 group and an $\text{-N(CH}_3)_2$ group, and Rc is chosen from a chlorine atom, and a bromine atom, or when Rd is an $\text{-N(CH}_3)_2$ group, Rc is chosen from $\text{C}_3\text{-C}_5$ alkenyl groups, or
- (4) - Rb and Rd are each a hydrogen atom, and
- Rc is chosen from halogen atoms, alkylamino groups, dialkylamino groups, alkyloxy groups, a trifluoromethoxy group, thioalkyl groups, $\text{C}_1\text{-C}_6$ alkyl groups, and trihalomethyl groups, or
- (5) - Rb and Rc are each a hydrogen atom, and
- Rd is chosen from halogen atoms, an ethylamino group, a diethylamino group, a methylethylamino group, alkyloxy groups, a trifluoromethoxy group, alkylthio groups, alkylsulphinyl groups, alkylsulphonyl groups, $\text{C}_1\text{-C}_6$ alkyl groups, a phenyl group, and trihalomethyl groups, or
- (6) - Rb is a hydrogen atom, **and**

- R_c is chosen from halogen atoms, alkylamino groups, dialkylamino groups, alkyloxy groups, a trifluoromethoxy group, thioalkyl groups, and C₁-C₃ alkyl groups, and
- R_d is chosen from halogen atoms, an amino group, alkylamino groups, dialkylamino groups, alkyloxy groups, a trifluoromethoxy group, thioalkyl groups, C₁-C₆ alkyl groups, and trihalomethyl groups, or

- (7) - R_c is a hydrogen atom, and
- R_b and R_d are each a methyl group, or

- (B) - R_a is an ethyl group, and
- R_b, R_c and R_d are defined as above in (2) to (7), and
 - R₅ is chosen from disubstituted methylenyl groups of formula:



wherein R₂ and R₄ are defined as above, or

- (C) - R₅ is a hydrogen atom,
- ~~- R_a, R_b, R_c, and R_d are defined as above in (2), provided that R''' is not an ethyl group when R_b and R_c are hydrogen atoms.~~
- R_a is a methyl group or an ethyl group, and
- R_b, R_c, and R_d are defined as above in (2), provided that R''' is not an ethyl group when R_b and R_c are hydrogen atoms.